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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/308,435	05/19/99	CARLSSON H	1103326-0560

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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1645	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/308,435	Applicant(s) Carlsson et al
	Examiner Portner	Group Art Unit 1645

☒ Responsive to communication(s) filed on *May 19, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-52* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3, 9, 10, and 38-44* is/are rejected.

☒ Claim(s) *4-8, 11-37, and 45-52* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-52 are pending.

Sequence Letter

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821 (a) (1) and (a) (2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

2. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.136. In no case may an applicant extend the period of response beyond the six month statutory period and the response period is the time set in this action. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

3. Acknowledgment is made of Applicant's bona fide attempt to place the instant application in sequence compliance.

4. Additional sequences were found by the examiner :

a. in Table 1, page 22 to page 25. All of the recited sequences need to be assigned SEQ ID NOs.

b. On page 26, Formula(s) I-III, that contain 4 or more amino acids;

must be assigned a SEQ ID NO to place the instant Application is sequence compliance.

Priority

5. Acknowledgment is made of applicant's claim for foreign priority, Swedish Application 981288-3, filed April 14, 1998, under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. PCT/SE99/00582, filed on April 9, 1999.

Specification

6. The use of the trademark at page 15, lines 5-9 have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claims 4-8, 11-37, and 45-52 are objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim must not depend from another multiple dependent claim and must depend from a prior claim in the alternative. See MPEP § 608.01(n). Accordingly, the claims 4-8, 11-37 and 45-50 are not [redacted] further treated on the merits.

Claim Rejections - 35 U.S.C. § 112

8. Claims 51-52 provide for the use of the claimed delivery system, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process

applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

9. Claims 51-52 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Please Note: Claims 38-44 are being read as vaccine claims. The polymer particles comprise a protein antigen that functions as a vaccine. The polymer particles have not been taught as being protective against any specific disease, therefore, the recitation of the word "vaccine" defines the protein contained in the delivery system as a protective antigen. The following scope of enablement rejection is being made in light of this reading of the claims.

11. Claims 38-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making polymer particles that comprise a protein

or lipoprotein, does not reasonably provide enablement for vaccines comprising any protein from any source or any Helicobacter protein from any species or any fragment of any Helicobacter protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims recite a polymer particle that comprises a protein antigen that is a delivery system for a vaccine. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity, in the case of the instantly claimed invention, the protection or prevention of infection would be against pathogenic *Helicobacter* (claims 39-44) or any pathogen ~~is~~ to which the recited protein is specific (claim 38). The specification teaches that the claimed antigen is immunogenic and stimulates a strong immune response when combined with cholera toxin.

The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity for prevention or treatment of H. pylori, using any protein or fragment thereof. The specification teaches that when using the delivery system with cholera toxin, a strong mucosal adjuvant, stimulates an enhanced immune response against HpaA antigen.

The art recognized standard for the determination of Helicobacter pylori infection is endoscopy and evaluation of tissue samples for the presence or absence of Helicobacter (see Buck et al, 1986). It is the examiner's position that a urease test is not directly indicative of, nor is it the art recognized standard for the evaluation of eradication of Helicobacter infection.

Data obtained from challenge experiments must demonstrate an art recognized standard of improvement over the control in order for the composition to be considered as being useful for treatment or prevention of infection. This information is essential for the skilled artisan to be able to use the claimed composition (vaccines) for their intended purpose of preventing *Helicobacter* infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

The prior art teaches that Helicobacter pylori vaccines are unpredictable, specifically, in the type of effect they will have on preventing or treating infection; the ability to reasonably predict the capacity of a single bacterial immunogen,

specifically catalase, to induce protective immunity is problematic.

a. In HP WORLD-WIDE, a publication from Brocades Pharma BV Leiderdorp, The Netherlands, February 1992, data was presented stating that immunization does not appear promising.

b. Parenteral immunization of specific pathogen free mice with *H. felis* gave no protection against gastric colonization; previous oral infection only delayed colonization (Heap,K, Australia).

c. The article also taught that "although intra-peyers patch immunization of killed *H. pylori* in rats shows that the gut mucosa can mount a vigorous immune response, oral immunization with either live or killed bacteria induced no significant serum or salival antibody response (Dunkley, M, Australia).

d. Blaser also warned that because of the possible autoimmune component of the disease the wrong vaccine could actually make things worse."

e.Rappuoli et al (European Journal of Gastroenterology and Hepatology, 1993, Vol.5, (suppl. 2) pages 576-578) teach that development of a vaccine against *Helicobacter pylori* would involve four major steps:

1) identification of the factors required for virulence;

2) large-scale production and characterization of the virulence factors;
3) development of appropriate animal models to test the virulence and immunogenicity of the molecules identified; and
4) identification of the type of immunity able to prevent infection and disease.

Unfortunately, the vaccine art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity.

f. Boslego et al teach a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum-antibody response is induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

Given the lack of guidance on how to obtain the desired effect using any protein or any fragment of any protein from any species of pathogen or any protein from any species of Helicobacter or any fragment of Helicobacter HpaA antigen to stimulate a protective immune response using the disclosed delivery system, the skilled artisan could not make and use the claimed invention. Without such information, one of skill in the

art could not predict which fragments or derivatives (claim 44 recites "substantially similar") out of the many fragments or derivatives possible would result in the desired effect.

One of skill in the art would be required to perform undue experimentation to identify any fragment or derivative which would be immunogenic and protective out of the many fragments or derivatives possible from the many sources of water insoluble protein antigens.

No evidence is of record showing that **any** polymer particle comprising any protein or fragment of the protein could confer the desired and claimed effect. No working examples are shown which convey the missing information. Therefore, the skilled artisan could not use **any** polymer particle as a vaccine against any pathogen or Helicobacter to obtain the desired effect of preventing or treating infection without undue experimentation.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 2, 3, 9, 38, ~~39, 43~~ and ~~44~~ are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 recites the phrase "in which the water insoluble protein is solubilized in the W phase using a solubilizing agent". The "insoluble protein" is **recited in the preamble** of the claim. The intended use of the particles is "[f]or use as a vaccine delivery system in which a water insoluble protein antigen is incorporated with particles". The recitation of an intended use does not provide the antigen for incorporation into the particles. The particles can be made without the incorporation of the protein. Reference to the preamble of the claim by narrative in the body of Claim 1, step (a), does not define step (a) of the method as incorporating the protein into the particles. The organic phase is defined to "comprise the matrix polymer" but the water phase is not defined to comprise anything other an aqueous element. Clarification of what reagents are being used is requested. "Mixing an aqueous phase (W)" --comprising a water insoluble protein and a solubilizing agent-- "with an organic phase", or an equivalent phrase, is suggested. Active voice method steps could obviate this rejection.

b. Claim 2 broadens the scope of claim 1 in the recitation of "more than one stabilizing agent" while claim 1 recites "a stabilizing agent". Claim 2 does not recite an upper limit for the number of stabilizing agents. How many solubilizing agents are being used is not distinctly claimed.

c. Claim 3, recites the phrase "the or each stabilizing agent". This is confusing. If more than one stabilizing agent is to be selected from the recited Markush group this should be clearly claimed. The Markush group is not a proper Markush group: --selected from the group consisting of---, is suggested.

d.Claim 9 depends from claim 2, which recites more than one stabilizing agent, but claim 9 only recites a single stabilizing agent. This is confusing. Claim 9 if amended to depend from claim 1 would be clearer. A claim that recites at least two stabilizing agents and has a claim that only recites a single agent does not distinctly claim Applicant's invention. Clarification is requested.

e. Claim 38 appears to have two components in the polymer matrix:

i.One being the protein antigen and

ii. the second being particles.

The recitation of the phrase "is incorporated with particles" defines the matrix as having two components. Applicant's invention is claimed as"A polymer particle". The claim as now recited does not distinctly claim Applicant's invention. Clarification of the relationship of the protein, particles and the polymer matrix is requested.

f. Claim 39 recites the phrase "a Helicobacter protein or fragment thereof". What the claimed fragments are, is not distinctly claimed. A fragment of a protein is not a protein but a polypeptide or even a single amino acid. The fragment, as claimed, is not even required to be immunogenic. Clarification of the invention is requested.

g. Claim 42 recites an abbreviation "HpaA". Abbreviations should be defined at their first appearing in the claims in order for the claimed invention to be clear.

h. Claim 43 recites the phrase "a fully lipidated form of HpaA" and depends from claim 42 which recites the phrase "a lipidated form of HpaA". It is not clear from the claim language

recited in claim 42 that the antigen is not fully lipidated. The claim language of claim 42 does not define the antigen as being partially lipidated. How the antigen of claims 42 and 43 differ is not clear.

i. The term/phrase "substantially similar to" in claim 44 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. How the claimed protein differs from SEQ ID No 2 or 4 amino acids 28-260 that is substantially similar is not distinctly claimed. What changes have been made has not been distinctly claimed.

OK

Please Note: The examiner is reading Claim 1 as a method of producing polymer particles that do not to contain a protein. The statements made with respect to the intended use of the particles are clarifying statements that do not recite positive claim limitations. A solution that contains a protein was not provided and used in the method of claim 1-3, 9-10.

Claim Rejections - 35 U.S.C. § 102

j. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Stated but not received

14. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Lee et al (1998). (This rejection could be obviated by submission of the Swedish priority document in English).

Lee et al disclose a method of producing a polymer particle for vaccine delivery system , wherein the method comprises the steps of:

a) mixing amphiphile lipopeptide in methanol (see 2.3.2) or ethanol (see 2.3.4) an (organic phase) to which was added an aqueous phase with vortexing (see page 175, col. 1, section 2.3.2 and col. 2, section 2.3.4). The amphiphile molecules served as a stabilizing agent and a solubilizing agent in the method for polymer particle production.

b) droplets were formed through thermal cycling of Hepes buffered saline dispersions in the presence of methanol or ethanol or by precipitation upon dilution of concentrated methanol solutions with an aqueous buffer (see section 2.3, page 175). The removal of organic solvent was accomplished through dilution in an aqueous solution followed by centrifugal driven filtration. The resultant particles were free of organic phase. (See section 2.3, page 175).

The reference inherently anticipates the now claimed invention.

15. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Goldstein et al (1997).

Other Claims w/ problem

Goldstein et al disclose a method of producing a polymer particle for vaccine delivery system (see page 35, col. 1, section 4., bottom half of paragraph), wherein the method comprises the steps of:

a) mixing lipopeptide and lipid ceramide, amphiphile in anhydrous DMF (organic phase) in water (aqueous phase). The emulsion (suspension) was vortexed (mixed). Amphiphiles served as a stabilizing agent and a solubilizing agent in the method for polymer particle production.

B) Additional water was added. The particles were pelleted and the supernatant removed. The particles were dried to remove residual liquid. (See sections 2.3.1 and 2.4.1 on page 26).

The reference inherently anticipates the now claimed invention.

16. Claims 1-3,9 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Fountain et al (US Pat. 4,610,868).

Fountain et al claim a process of producing polymer particles (lipid matrix carriers) for vaccine (drug) delivery systems (see claims 50-**51**, 56,68, 70, 71, **83**, 95-101.) (Instant invention claim 1) The disclosed methods steps comprise:

a.) Mixing an aqueous phase (see claim 50, section b, where an aqueous phase is agitated) and an organic phase (see claim 50, section a) together with a solubilizing agent (see claim 50, section (a) "amphipathic compound").

b.) droplets are formed (globular structures, claim 50, step b, 4 lines from the bottom of this section), followed by removal of the organic solvent (see claim 51 dependent upon claim 50).

(Instant invention claims 2-3 and 9) The reference claims the addition of a second stabilizing agent, a surfactant to the amphipathic compound (see claims 56, 67 and 68). The mixture used in the claimed method therefore comprises more than one stabilizing agent. The additional stabilizing agent claimed is sorbitan mono-oleate, an example of a fatty acid ester of sorbitan (see claim 68).

Incorporation of lipoproteins in the polymer particles produced is claimed (see claim 83).

Fountain et al anticipate the now claimed invention.

Please Note: The following art rejection over Maitra et al and Wu et al are being made in light of the 35 U.S.C. 112, second paragraph rejection made above, wherein the presence of a water insoluble protein is not required to be present in the product produced by the method.

17. Claims 1 and 2 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Maitra et al (US Pat. 5,874,111).

Maitra et al disclose and claim a method of making a polymeric particle, wherein the method comprises the steps of:

a. Mixing an aqueous phase (see section ii), an organic phase (oil, section 1 of claim 1) with), a stabilizing agent (surfactant, section 1 of claim 1) and solubilizing agent (a initiator that is a water soluble perdisulphate sols and TMED, see claims 1 and 6) to obtain droplets (claim 1, section 1) that are contained in an emulsion (see section iii of claim 1) which is polymerized into a polymer matrix.

b. The polymerized droplets are dried to remove solvent and unreacted material. The dried product is dispersed in an aqueous buffer (see claims 11-12) to separate out any surfactant left, as well as any other toxic materials (organic phase) from the polymer particles (see claim 1, sections iii, iv, v and vi). Removal of toxic subststances is accomplished using a buffer that comprises calcium chloride (see claim 10)

The claimed polymer particles are made from vinyl pyrrolidone (see claim 1, section ii and claim 3) in association with sulphosuccinate surfactant (see claim 8).

The reference anticipates the now claimed invention.

18. Claims 1,2,3, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al (US Pat. 5,025,004).

Wu et al claims a product produced by a method and a method of producing the product, wherein the product is polymeric particles produced by the methods steps of:

a) mixing an aqueous phase (see claim 6, process step II) with an organic phase to form an emulsion that comprises an organic solvent, an insoluble polymer, a stabilizer and a stabilizer (see claim 6, that defines the organic phase, section I)

b) forming droplets through passing the polymer emulsion through a microfluidizer (claim 6, section III) and removing the organic solvent from the emulsion, followed by drying the polymer matrix.

The disclosed and claimed organic solvents are methylene chloride, ethylene dichloride, chloroform or isopropanyl plus ethyl acetate

The disclosed and claimed water insoluble polymer is any one of the recited polymers shown at col. 23, lines 46-65 and mixtures of the recited polymers. Among the polymers claimed separately or in a mixture and cellulose acetate succinate and poly(4-vinylpyridine).

~~Solubilziers~~ Solubilizers are disclosed and claimed include polyoxy-ethylene sorbitan monolaurate, poloxamer, polyoxyethylene sorbitan tristearate, polyoxyethylene sorbitan monostearate and mixtures thereof.

The stabilizing agents claimed include phospholipids and other hydrophobic surfactants. (See col. 24, lines 3-10).

The reference anticipates the now claimed invention.

19. Claims 38-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Bolin et al (WO96/38475).

Bolin et al disclose polymer particles as a vaccine delivery system that comprise Helicobacter pylori HpaA lipoprotein. The polymer particles disclosed for the vaccine delivery are liposomes, ISCOMS, cochleates and polymer microspheres of degradable or non-degradable materials (see page 11, lines 8-15).

The Helicobacter protein is a 29 kDa lipoprotein that was used as an therapeutic oral immunogen that lead to significant reduction of colonization of H.pylori in mice (see page 4, lines

6-9). The amino acid sequence disclosed comprises amino acids 1-260 or 28-260 of SEQ ID NOs. 2 or 4 (see page 6, lines 8-10). SEQ ID NO. 2 is taught to have a serine at residue number 222, and SEQ ID NO 4 has arginine at residue 222, otherwise the sequences are identical.

In view of the disclosure of Bolin, the reference inherently anticipates the now claimed polymer particle vaccine delivery system that comprises a Helicobacter pylori lipidated form of HpaA of SEQ ID NOs 2 or 4 having amino acid positions 28-260.

20. Claims 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Michael et al (US Pat. 5,629,001).

Michael et al claim a polymer particle that comprises a Helicobacter pylori antigen (claim 3, col. 8, line 18), wherein the antigen is an immunogen of the whole Helicobacter pylori (see claims 1 and 3) or is whole killed Helicobacter pylori (see claim 6). Helicobacter pylori whole killed antigen comprises water insoluble protein antigens. The polymer particle claimed is made from a water based emulsion of ethyl acrylate methacrylic acid copolymer (see claim 2) or from polyvinylpyrrolidone (see claim 16).

The reference inherently anticipates the now claimed polymer particle that comprises a water insoluble protein antigen of Helicobacter pylori.

Conclusion

21. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

22. Czinn et al (US Pat. 5,538,729) teach the use of liposomes, micro capsules and ISCOMs for the administration of a Helicobacter antigen to a host (see col. 4, lines 64-67 and col. 5, lines 1-3).

23.Buchel et al (US Pat 4,134,725) is cited to methods of making particles.

24.Chaiko et al (US Pat. 5,948,263) is cited to show the use of *inorganic salts* in a method of making a polymer

25. Conte et al (US Pat. 5,780,057) is cited to show a polymer particle that comprises both polyvinyl pyrrolidone and sulphosuccinate (see claims 1 and 10).

26. Elton et al (US Pat. 5,104,.904) is cited to show polymer dispersion of polymer particles that comprise both polyvinylpyrrolidone and anionic sulphosuccinate (see description of invention).

27. Illig et al (US Pat. 5,330,740) is cited to show a polymeric material for the visualization of the gastrointestinal tract.

28.Martin et al (US pat. 4,344,934) is cited to show polymer particles that comprise both polyvinylpyrrolidone and sulfo succinate (see claim 17).

29. Morrison et al (US Pat. 5,827,531) is cited to show a method of producing polymer particles

30. Hunter et al (5,622,649) is cited to show the use of aqueous, organic, stabilizers and surfactants in the production of droplet emulsions useful in stimulating an immune response.

31. Andrianov et al (5,529,777) is cited to show a polymer particle that comprises a protein.

32. WO96/36317 is cited to show a method of removing solvent from a micro droplet that results in a solvent free micro particle.

33. WO95/11010 and WO95/11009 are cited to show a method of making polymer particles.

34. **Plaut et al** (US Pat. 5,534,544) I s cited to show surfactants and emulsifying agents that inhibit Helicobacter pylori growth.

35. WO99/52550 is cited to show polymer particle vaccine delivery system.

36. WO96/40893 is cited to show Helicobacter pylori antigens and the suggestion to include them in polymeric particles.

37. Yager et al (US Pat. 5,851,536) is cited to show therapeutic drug delivery compounds that is duplicative of the applied references of Lee and Goldstein applied above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
September 26, 2000

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TEC[illegible]